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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,909	07/17/2003	Wayne Vaccaro	QA0266 NP	2136
23914	7590	05/21/2004	EXAMINER	
STEPHEN B. DAVIS BRISTOL-MYERS SQUIBB COMPANY PATENT DEPARTMENT P O BOX 4000 PRINCETON, NJ 08543-4000			AULAKH, CHARANJIT	
			ART UNIT	PAPER NUMBER
			1625	

DATE MAILED: 05/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/621,909

Applicant(s)

VACCARO ET AL.

Examiner

Charanjit S. Aulakh

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 13 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-12 and 14-34 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. ____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 2.
- ☒ Interview Summary (PTO-413)
Paper No(s)/Mail Date. 12 May 2004.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: ____.

DETAILED ACTION

1. Claims 1-34 are pending in the application.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 1-12 and 14-34, drawn to compounds of formula of claim 1 where both rings A and B represent phenyl groups and one of R1 or R2 (variable Z) represents heteroaryl group, pharmaceutical compositions containing these compounds and a method of using these compounds, classified in class 548, subclass 195.
- II. Claims 1-34, drawn to compounds other than defined above for group I, pharmaceutical compositions containing these compounds and a method of using these compounds, classified in classes 540, 544, 546, 549, 560, 564.

3. The inventions I and II as defined above are patentably distinct, each from the other since they are structurally so divergent that a reference showing compounds of invention I would not render compounds of invention II prima facie obvious. Search required for e.g ; compounds of invention I in class 548 is not the same search required for e.g ; compounds of invention II in classes 540, 544, 546, 549 etc. and therefore, constitutes a burdensome search.

4. During a telephone conversation with the applicant's attorney, Ms. Laurelee Duncan on May 12, 2004, a provisional election was made with traverse to prosecute the

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invention of group I (compounds of formula F on page 216 as species), claims 1-12 and 14-34. Affirmation of this election must be made by applicant in replying to this Office action. Claim 13 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. It is of note that group II is subject to further restriction based on the values of rings A and B as well as variables R1 and R2 in the future applications.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 18-20 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following eight different factors (see *Ex parte Foreman*, 230 USPQ at 547; *Wands*, *In re*, 858 F. 2d 731, USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed :

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Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on at least four of the above mentioned eight factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, the state of the prior art and the breadth of claims.

The specification mentions on page 1 that the instant compounds are non-steroidal compounds which are glucocorticoid receptor (GR) modulators. The specification also teaches that glucocorticoids exert their anti-inflammatory activity via inhibition by GR of the transcription factors NF-kappaB and AP-1 which is termed transrepression (see page 2, lines 1-5). In addition to causing transrepression, the interaction of glucocorticoids with GR can cause GR to induce transcription of certain genes, which is termed transactivation (see page 2, lines 20-23). This transactivation has been suggested to be responsible for the side effects of glucocorticoid therapy (see last paragraph on page 2). There is no teaching in the specification whether the instant compounds cause transrepression, transactivation, inhibit transrepression or inhibit transactivation. The utility of the instant compounds will be different based on agonist versus antagonist activity for transrepression or transactivation. There is no teaching either in the specification or prior art reference showing well known utility of prior art compounds which inhibit transrepression, cause transactivation or inhibit transactivation. There are no working examples present in the specification showing

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efficacy of the instant compounds in vivo in known animal models of any disease state. The instant compounds of formula of claim 1 encompasses hundreds of thousands of compounds based on the values of variables Ra to Ri, R and z and therefore, in absence of such teachings, guidance or presence of working examples, it would require undue experimentation to assess their agonist versus antagonist activity for transrepression or transactivation and hence their utility.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-12 and 14-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In independent claims 1 and 24-27, the terms ---stereoisomers and prodrug ester ---are indefinite since it is not clear which specific stereoisomer or prodrug ester is being referred here and furthermore, the steps for preparing them are not defined. Also, the terms ----heteroaryl and cycloheteroalkyl --- used for various variables are indefinite since the size of the ring, number and types of heteroatoms present in the ring are not defined.

In claim 18, the terms ---preventing and inhibiting --- are indefinite since the degree of prevention or inhibition (20%, 40%, 60%, 80% or 100%) is not defined.

In claim 18, the term ----GR-associated disease --- is indefinite since these diseases are not defined and furthermore, it is not clear how they are associated with GR?

In claim 25, the value of variable Z1 is not defined.

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In claim 26 on page 259, the same compound is being treated with an amine (see lines 1-6) and with a base (see lines 7-15). It appears that something is missing. Also, the variable R1 does not appear in the formula or defined in the claim.

Allowable Subject Matter

10. The following is a statement of reasons for the indication of allowable subject matter:

The instant compounds directed to the elected group are allowable over the prior art since they are neither disclosed nor obvious over the prior art. In the art, Pradines (Antimicrob. Agents and Chemother. , cited on applicants form 1449) discloses compounds BG 1049, BG 1050 and BG 1051 (see table 1 on page 2065) which are closely related to the instant compounds. However, the compounds of Pradines differ from the instant compounds in having one of R1 and R2 variables as H and these compounds have been excluded by a proviso in the instant claim 1 (see page 208, lines 8-15).

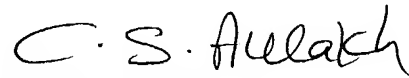
11. Claims 1-4, 7, 8 and 18-34 are objected as containing non-elected subject matter.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Charanjit S. Aulakh
Primary Examiner
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